510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k051299

B. Purpose for Submission:
New Device

C. Measurand:
Human anti-IgD antibodies.

D. Type of Test:
Quantitative nephelometry

E. Applicant:
The Binding Site, Ltd.

F. Proprietary and Established Names:
Human IgD Liquid Reagent Kits for use on the Behring BNII Analyzer

G. Regulatory Information:
1. Regulation section:
   21 CFR 866.5500 Immunoglobulins (A, G, M, D, E) Immunological Test System
2. Classification:
   II
3. Product code:
   CZJ – IgD, Antigen, antiserum, control
4. Panel:
   Immunology 82

H. Intended Use:
1. Intended use(s):
   This kit is intended for measuring human Immunoglobulin D (IgD) in serum as an aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.
2. Indication(s) for use:
   Same as Intended use.
3. Special conditions for use statement(s):
   The device is for prescription use only.
4. Special instrument requirements:
   The device is designed to be used with the Dade Behring BN™II Analyzer (k943997).

I. Device Description:
The device consists of a Human IgD Standard, Low Control (Human IgD Control), IgD Control (Human IgD High control), IgD Latex Reagent, IgD Supplementary Reagent, and the instructional leaflet. The Human IgD Latex Reagent is monospecific antiserum coated onto polystyrene latex and is supplied in a stabilized liquid form. The IgD Controls and Calibrator (standard) consist of pooled human serum, stabilized in liquid form.

J. Substantial Equivalence Information:
1. Predicate device name(s):
   Human Immunoglobulin D Bindarid™ Radial Immunodiffusion Kit.

2. Predicate 510(k) number(s):
   k913671
3. Comparison with predicate:

Similarities		
Item	New Device	Predicate
Intended Use	Same	Same
Results	Quantitative interpretation	Same
Antigen	Same	Same
Sample type	Human Serum	Same
Relative sensitivity	100% with myeloma patients vs. norm sera	Same

Differences		
Item	New Device	Predicate
Basic Technology	Nephelometry. Light scatter	Radial Immunodiffusion
Sample preparation	Automated	Manual, dilute in 7% BSA
Sample dilution	1:100	None
Controls	2 levels	Single level
Interferences	None w/ Bilirubin, Intralipid & Hemoglobin	No Data
Analytical Range	1.3 - > 4150 mg/L	4.4 - 9144 mg/L
Lowest detectible limit	1.3 mg/L	5 mg/L
Antisera specificity	< 9% cross reactivity w/ IgG, IgM, and IgA	No Data
Shelf life stability	Unopened: until expiration date @ 2-8 ^{o}C Opened reagents: 8 wks @ 2-8°C	Same 1 week @ 2-8°C

K. Standard/Guidance Document Referenced (if applicable):
   None provided.
L. Test Principle:
   The Human IgD Liquid Reagent Kit (BNII) utilizes nephelometry to measure the light scattered by particles in solution. Monospecific antiserum is coated onto stabilized latex particles of a sufficient size. The latex particles are then incubated with dilutions of patient sera. If IgD is present in a soluble form it will form insoluble immune complexes which are light-scattering. The amount of light-scatter measured is directly proportional to the concentration of IgD in the sample when the antibody is in excess. The concentration of IgD in the sera is automatically calculated by the instrument by comparing the amount of light-scattering for each unknown sample to that of a calibration curve.

M. Performance Characteristics (if/when applicable):
   1. Analytical performance:

a. *Precision/Reproducibility:*
   Three samples were tested twice a day for a total of 21 days. The "High" sample is between 75-95% of the upper limit of the measuring range. The "Medium" sample is close to the medical decision level (positive/negative cutoff) and the "Low" sample is between 140-180% of the lower limit of the measuring range.

Sample	Mean mg/L	Total		Within-run		Between-run		Between-day	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
High	183.26	13.21	7.2	8.0	4.4	7.18	3.9	7.68	4.2
Med	162.51	14.47	8.9	4.1	2.50	8.4	5.10	11.1	6.8
Low	9.29	1.46	15.7	0.98	10.6	0.49	5.3	0.96	10.3

b. *Linearity/assay reportable range:*
   Study design: Three serum samples were serially diluted to cover the measuring range of the assay and tested on a single kit. Two of the samples were further tested on two other kit lots (one per kit). The IgD concentration of the samples ranged from 0.83-228 mg/L. A linear regression analysis of the data for all samples run on each kit gave the following equations: $y = 1.0081x - 0.0948$, $R^2 = 0.9911$ (three samples); $y = 1.0064x - 0.4857$, $R^2 = 0.9997$; and $y = 0.9818x - 0.595$, $R^2 = 0.9967$. The recovery for all samples ranged from 74.17% to 125.88%.

	Measuring Range	
	mg/L	Sample dilution
IgD	6.5-207.5	1:100
	130-4150	1:2000

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   The calibrators are traceable to the NIBSC 67/037 standard.

d. *Detection limit:*
   Ten replicates of two samples with concentrations equivalent to 140% and 200% of the lower limit of the standard curve (6.18mg/L) were tested. The mean concentrations were 9.3 and 13.3 mg/L and the %CVs were 7.3% and 3.3%, respectively.

e. *Analytical specificity:*
   i. <u>Interference</u> by endogenous substances: Aliquots of a sample containing 8.4 mg/L IgD at the minimum sample dilution of 1:20 were tested after the addition of 0.5% triglycerides/intralipids, 5g/L hemoglobin, or 200 mg/L bilirubin. Minimal interference was detected with the substances (+2.4%, +7.7% and -7.1% from the assigned value, respectively).
   ii. <u>Cross-reactivity</u> with other antibodies were determined by the addition of pure preparations of different immunoglobulins to two low control sera, to give a final concentration of 2g/L for IgA1&2 (Kappa and Lambda), 3g/L IgG, and 1g/L IgM (Kappa & Lambda). All demonstrated a < 9% difference when compared with an analogous blank (control sera spiked

with an equivalent volume of saline).

iii. <u>Antigen excess</u> was analyzed by running an eight point curve using the IgD standard at a concentration range of 55-8857 mg/L at a 1:100 dilution. Clinical samples were tested at 1:100, 1:400, 1:2000, 1:8000, and 1:40,000 and 1:160,000 dilutions. Nine samples were shown to be in antigen excess at 1:100, and 2 at 1:400. For polyclonal samples, the assay was determined to have an antigen excess capacity of 3.5 g/L, however no antigen excess at a 1:2000 dilution was observed with 24 separate myeloma samples.

f. *Assay cut-off:*
The assay cut-off was determined to be the upper limit of 121 sera from normal healthy adults in the United Kingdom (17-59 years old) and was 152.7 mg/L. Twenty-three myeloma samples tested and all fell outside the normal range of <153 mg/L.

2. <u>Comparison studies:</u>

a. *Method comparison with predicate device:*
Thirty normal and twenty-three myeloma patient sera were tested on both the Human IgD Liquid Reagent Kit and the Human Immunoglobulin D Bindarid™ Radial Immunodiffusion Kit. Comparative results are summarized below.

		Bindarid RID		
		(+)	(-)	Total
BNII IgD Liquid Reagent kit	(+)	23	0	23
	(-)	0	30	30
	Total	23	30	53

Positive percent agreement: 100% (23/23)
Negative percent agreement: 100% (30/30)
Overall agreement: 100% (53/53)

Study results were also analyzed by linear regression. Even though qualitatively both assays had 100% agreement but quantitatively, there was a bias between the two assays with y = 1.2324x - 30.963 mg/L (y = BNII IgD x 0.6* and x = IgD RID) and a correlation coefficient (R^2) = 0.9221. The observed bias was primarily due to different reference materials used for assay calibration. Binding Site IgD RID kit is calibrated to an alternative reference material whereas the BNII IgD is calibrated to the NIBSC 67/037 standard. The two assays were found to differ by a factor of 0.6 which was used to adjust the results of the BNII IgD.

b. *Matrix comparison:*
Both assays use human serum as a matrix.

3. <u>Clinical studies:</u>

a. *Clinical Sensitivity and specificity*
Thirty normal and twenty-three myeloma patient sera were tested on both the Human IgD Liquid Reagent Kit

		Diagnosis		
		(+)	(-)	Total
BNII IgD Liquid	(+)	23	0	23
Reagent kit	(-)	0	30	30
	Total	23	30	53

Clinical sensitivity: 100% (23/23)
Clinical specificity: 100% (30/30)

4. <u>Clinical cut-off</u>**:**
See Assay Cut-off.
5. <u>Expected values/Reference range:</u>
Expected value in the normal population is <153 mg/L. The sponsor cited literature that states that IgD levels are raised in Hyperimmunoglobulineamia D syndrome (HIDS) where results increase greatly during a febrile attack to greater than 140 mg/L.

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:
The submitted information in this premarket notification is complete and supports substantial equivalence decision.